

# Nano-Particles and Targeted Delivery using Ultrasound

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## **Founder Ultra Imaging LLC**

ASTM, NCI - NCL, NIST and FDA  
Joint Workshop

## Disclosure:

Ultra Imaging LLC

University of Illinois at Urbana-Champaign

- Office of Technology Management
- Beckman Institute for Advance Science and Technology
- Center for NanoScale Technology

Aloka Company, Ltd.

BioCrystal Ltd.

# Outline

## I. Current Development

## II. Contrast Agents - Nano Particles

- a) Gadolinium Oxide Microspheres
- b) Lipid Based Drug Delivery Nanoparticles
- c) Silica Nanoparticles

# Current Development

- Imaging Machinery [US5,908,388; US5,485,841]
  - Small Ultrasonic Device for Imaging & Drug Delivery using Ultrasound Sensitive Nanoparticles



# Current Development

- Gadolinium Oxide Microspheres
- Lipid Based Nanoparticles
- Silica Nanoparticles

# Current Development

- Contrast Agents

- Multi Modal

- CT – MR – US – PET - SPECT

- US6797257

- Microsphere with embedded particulates (GdO, MnO ...)

- Neutron Capture Therapy

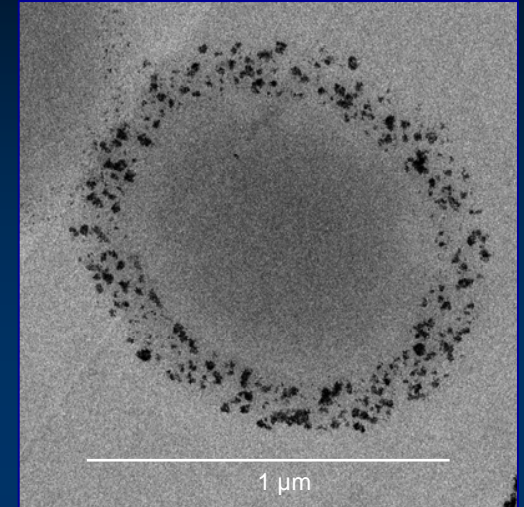
- » High Neutron Capture Cross Section

- » Tumor targeted radiation therapy

- gliomas

- Dextranized Gadolinium Oxide

- » 7nm

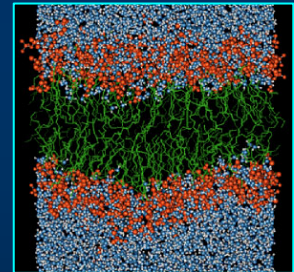
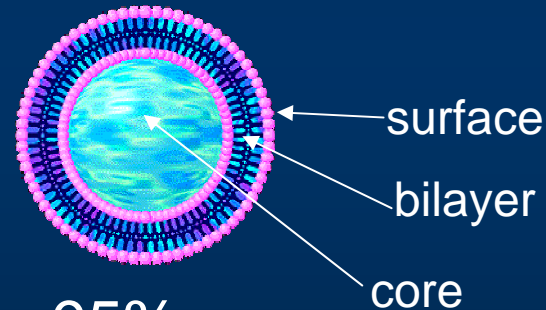


# Controlled Release Nano Particles (CR-NPs)

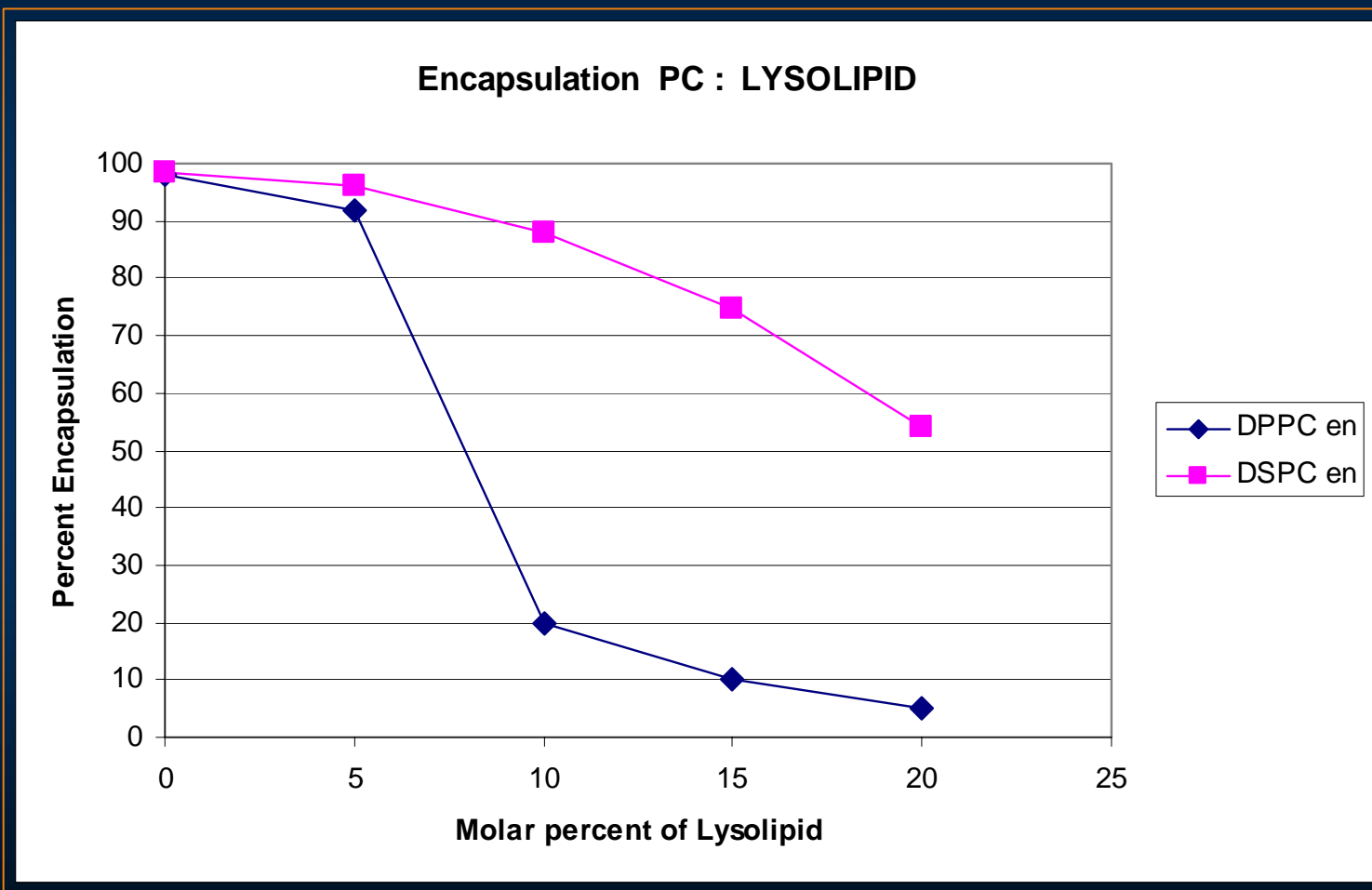
- Controlled Release Nanoparticles (CR-NPs)
  - Patent pending
  - Controlled release using ultrasound
  - Differential release
  - Targeting
    - » IGF-R1
    - » Mucin - 1
    - » Annexin - V
    - » VCAM -1
  - Loading
    - » Urokinase
    - » Docetaxel

# Loading Phase

- Encapsulation of Drugs into Nano-Particles
  - Size : 30 nm – 200 nm
  - Encapsulation Range : 35 – 95%
    - Dependent upon formulation



# Loading Characteristics



# Targeted Drug Delivery Method



# Targeted Drug Delivery Technology



- *Point and Shoot Method*

- *Inject*

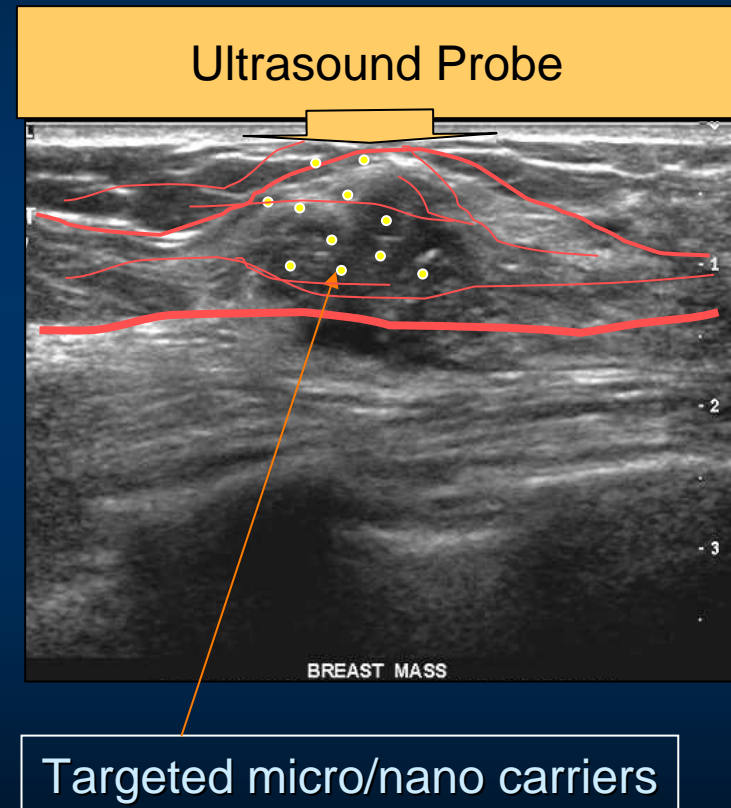
- entrapped cancer drugs in small micro or nano carriers functionalized with cancer seeking antibodies

- *Image*

- the targeted cancer cells/tumor with ultrasound

- *Release*

- the encapsulated drug using the ultrasound imaging system



# Point



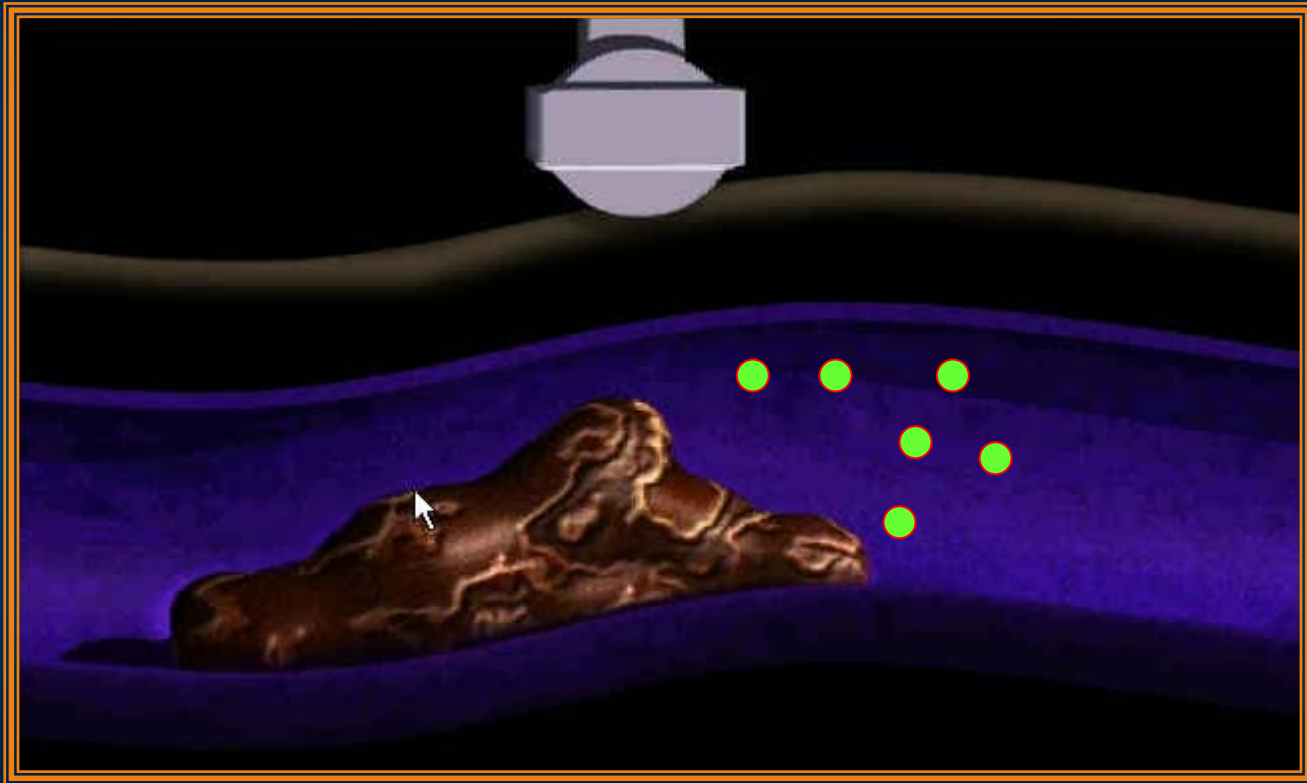
# Point + Injection



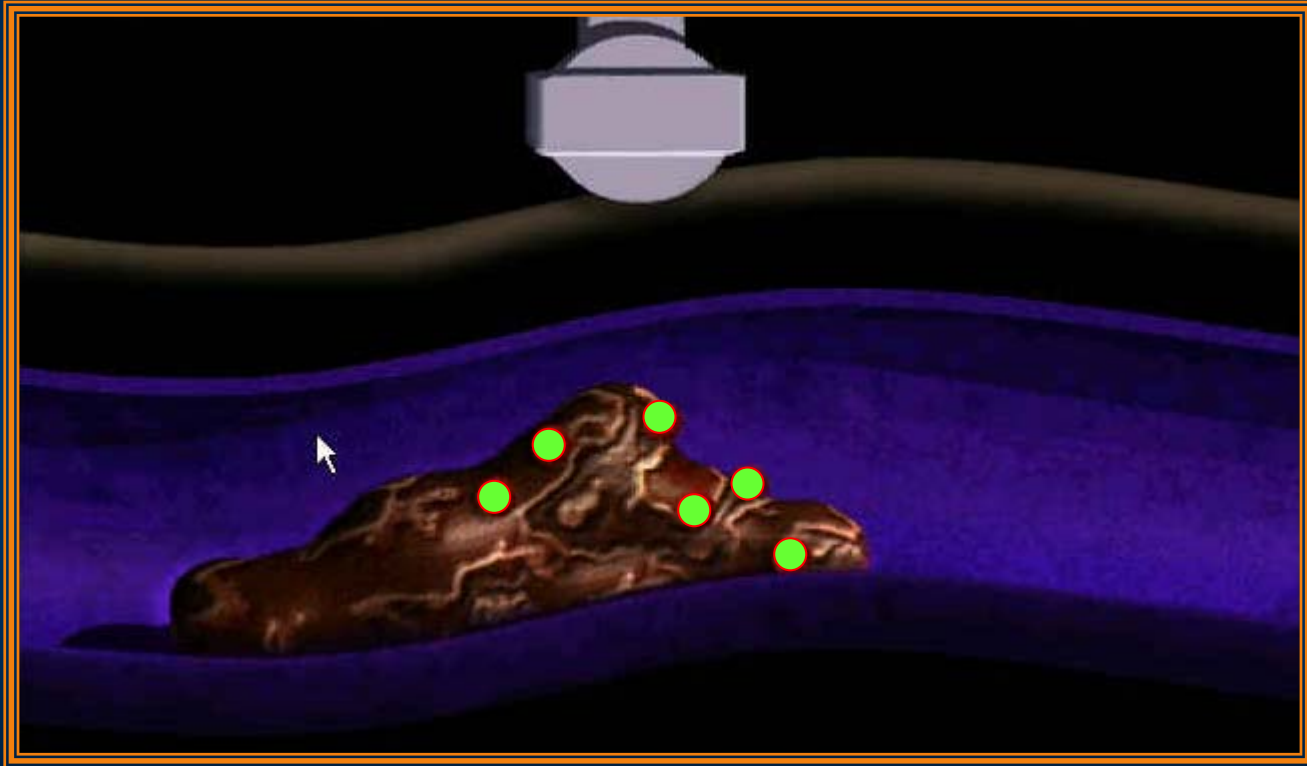
# Point



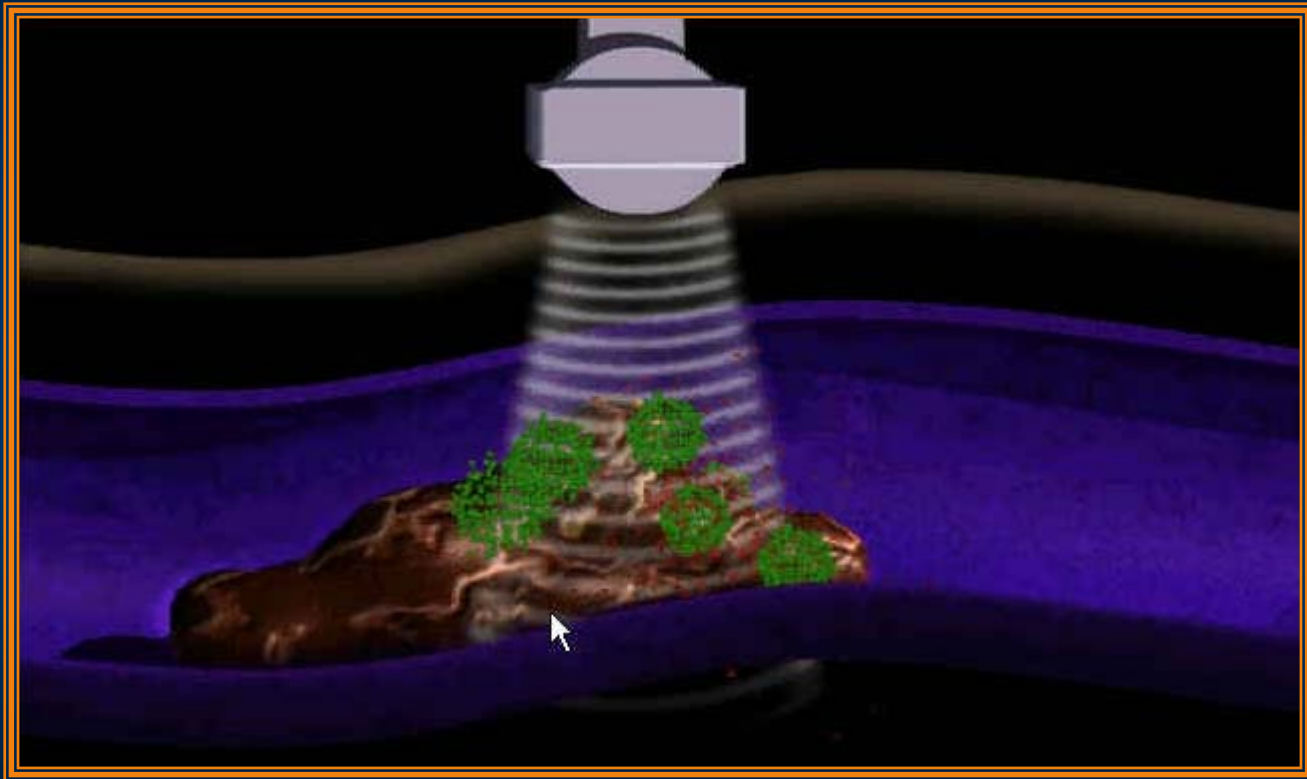
# Point



# Point + Attached



# Shoot



# Targeting

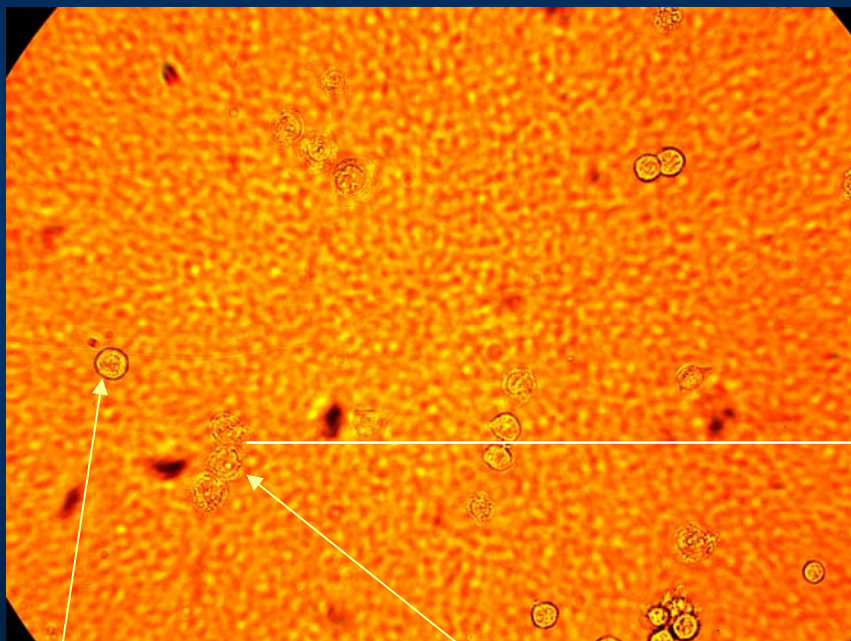


# Targeting

Mini Opticell



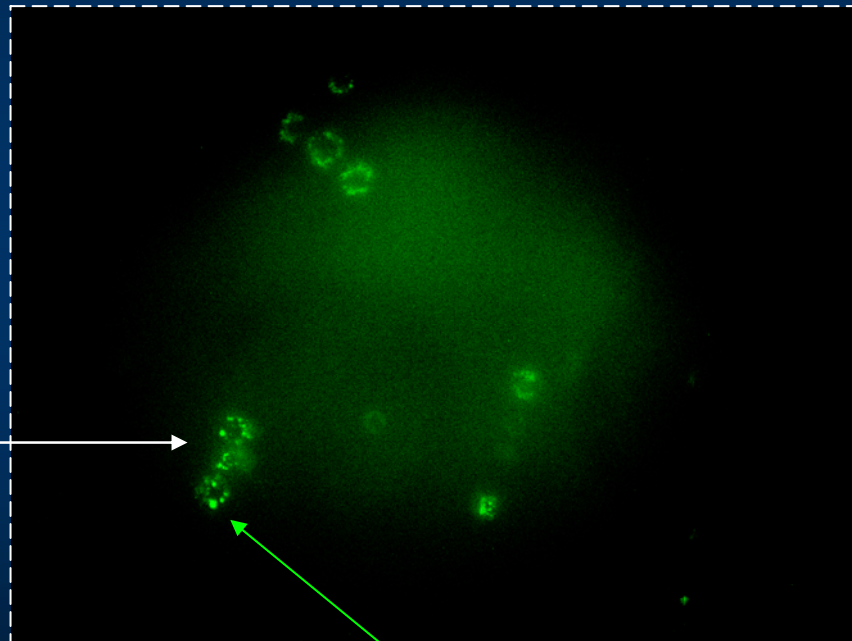
Light Microscope Image



Floating cells

Cancer cells adhering to Opticell membrane

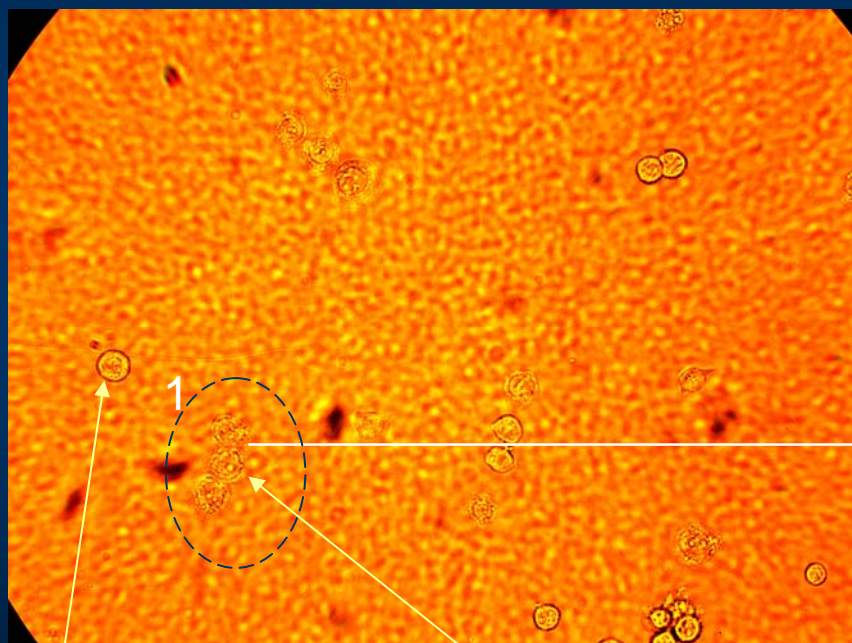
Fluorescence Microscope Image



Nanoparticles with IGF-R1 targeting

# Targeting

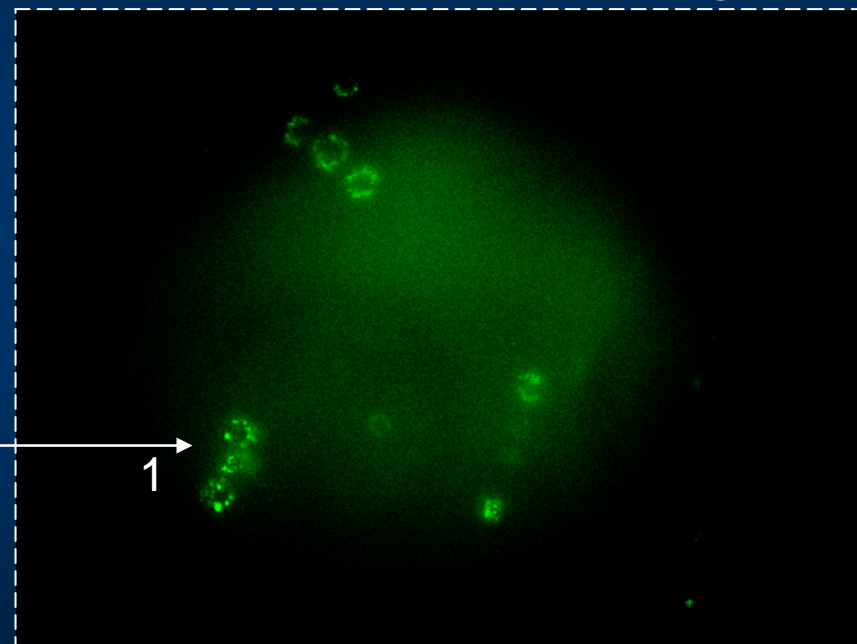
Light Microscope Image



Floating  
cells

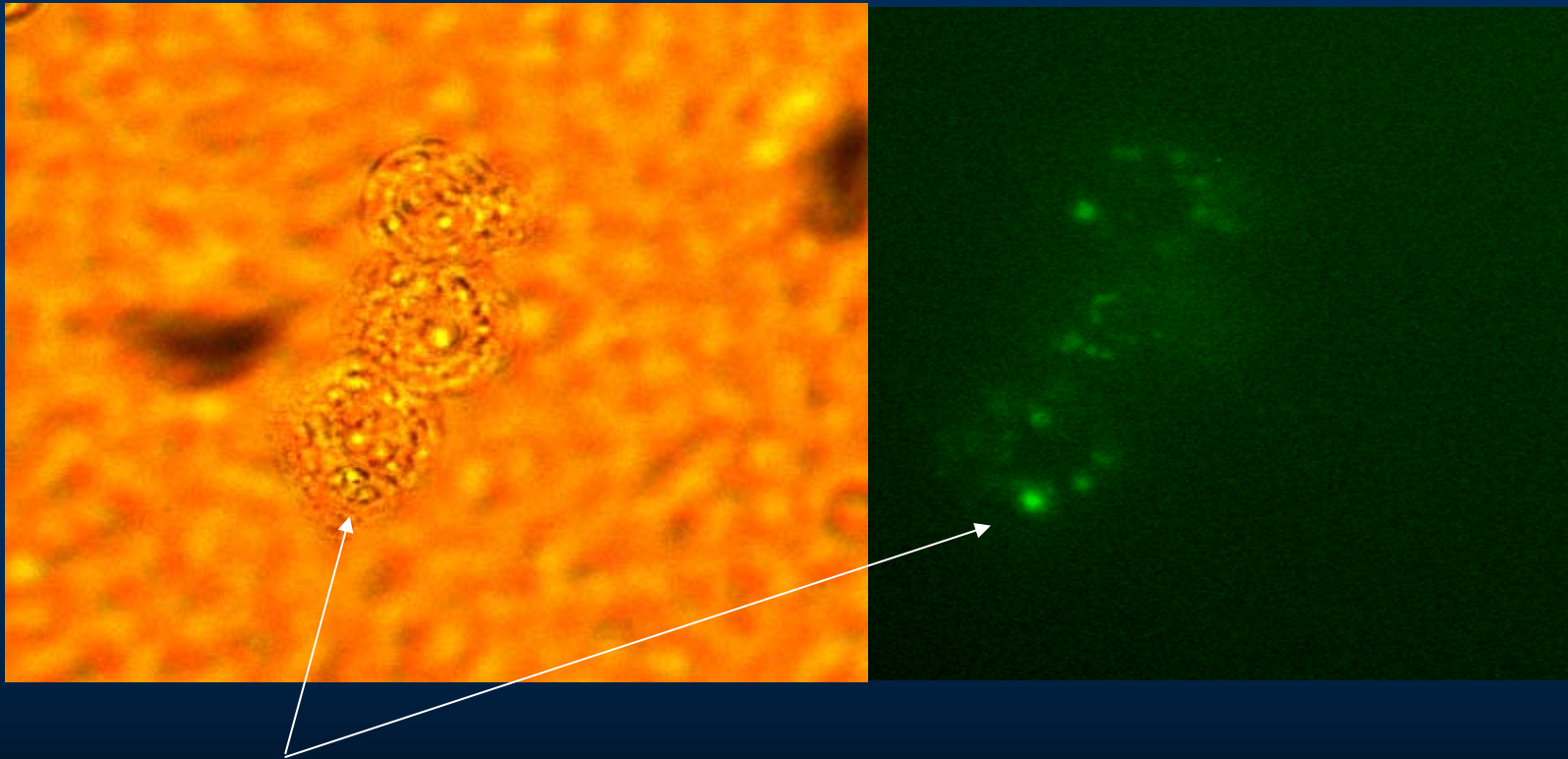
Cancer cells adhering to  
Opticell membrane

Fluorescence Microscope Image



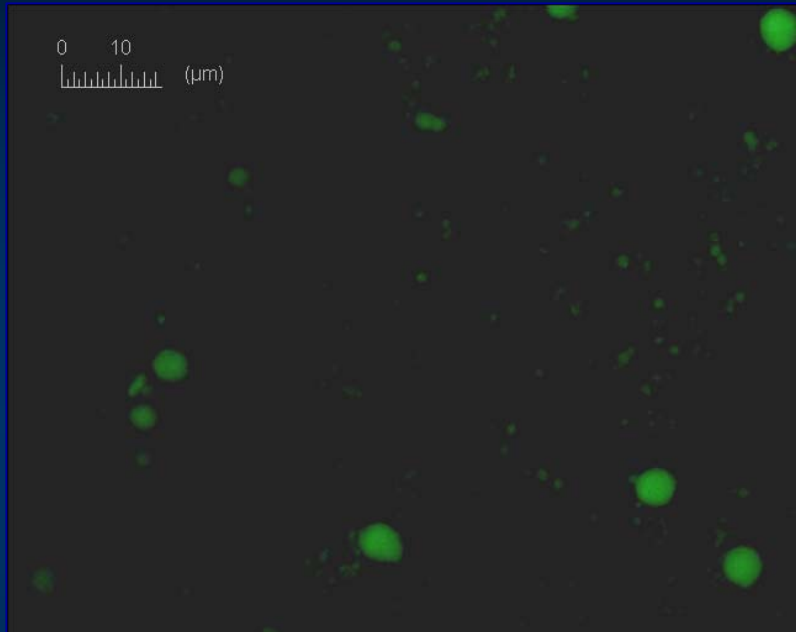
nanoparticles

# Regional Enlargement 1



# Load Releasing Characteristics

# Ultrasound Release using Carboxyfluorescein



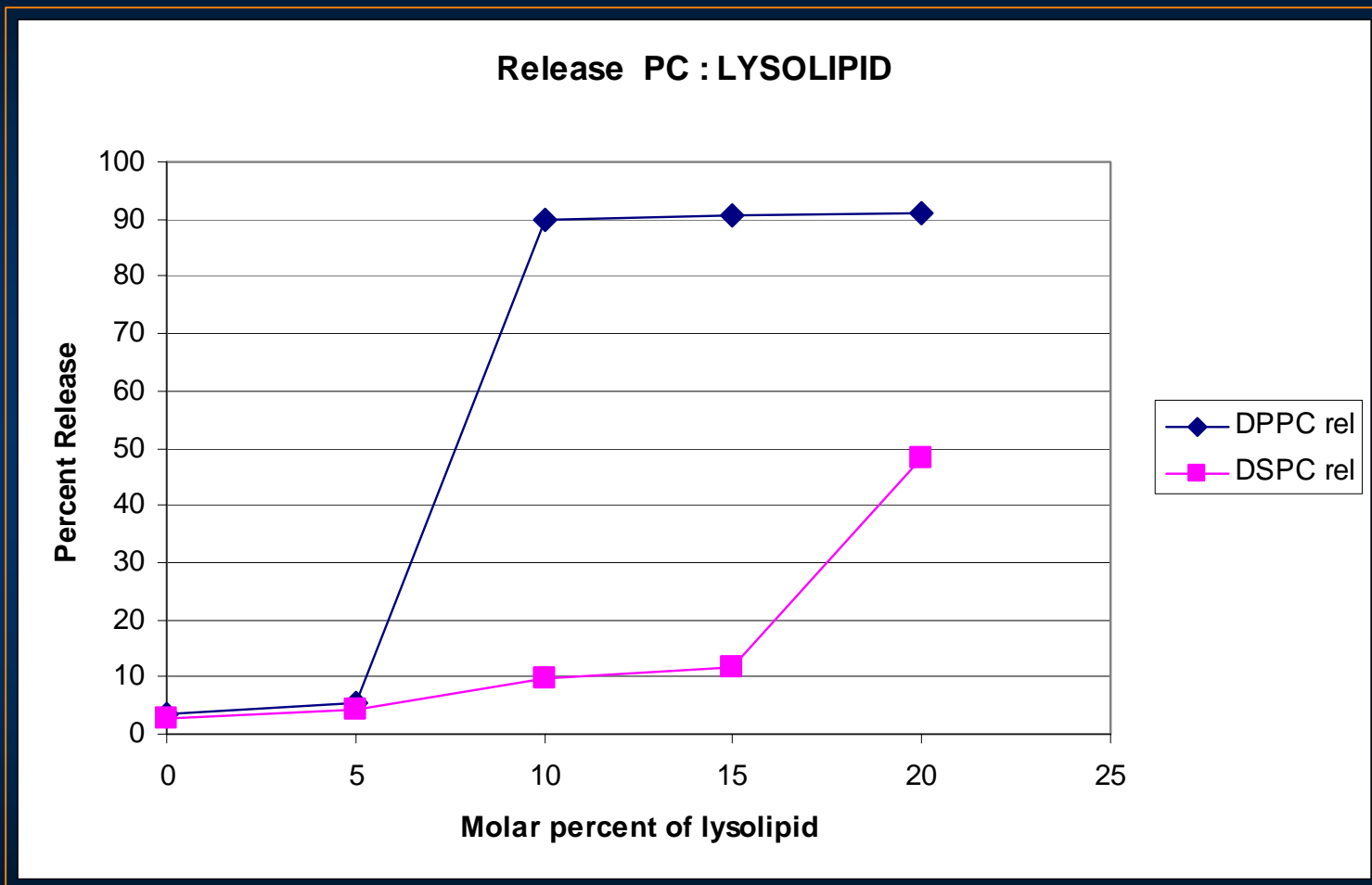
**BEFORE**  
Insonation



**AFTER**  
Insonation

Watkin, 2003

# Percent Release @ 7.5MHz Linear Array



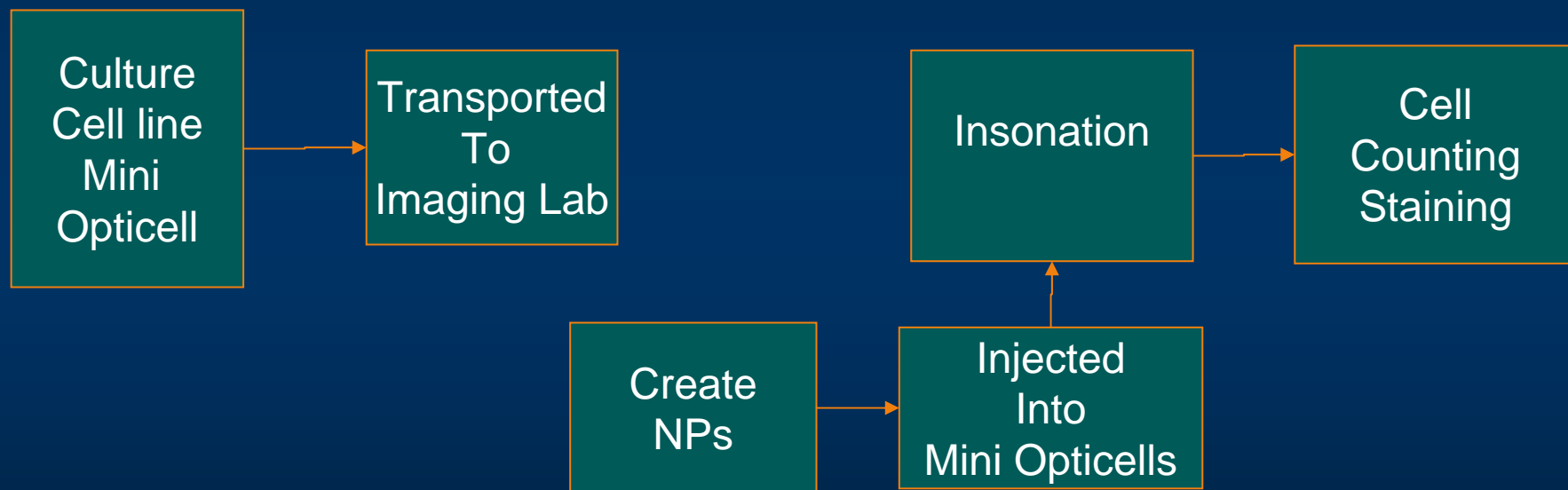
Watkin & Gosangari, Controlled Release Society, Miami, FL, June 2005

# In Vitro Testing

# In Vitro Test Cell Lines

- HT 29 Colon cancer
- HCT- 116 Colon Cancer
- MCF-7 Breast Cancer
- SCC-9 Squamous Cell

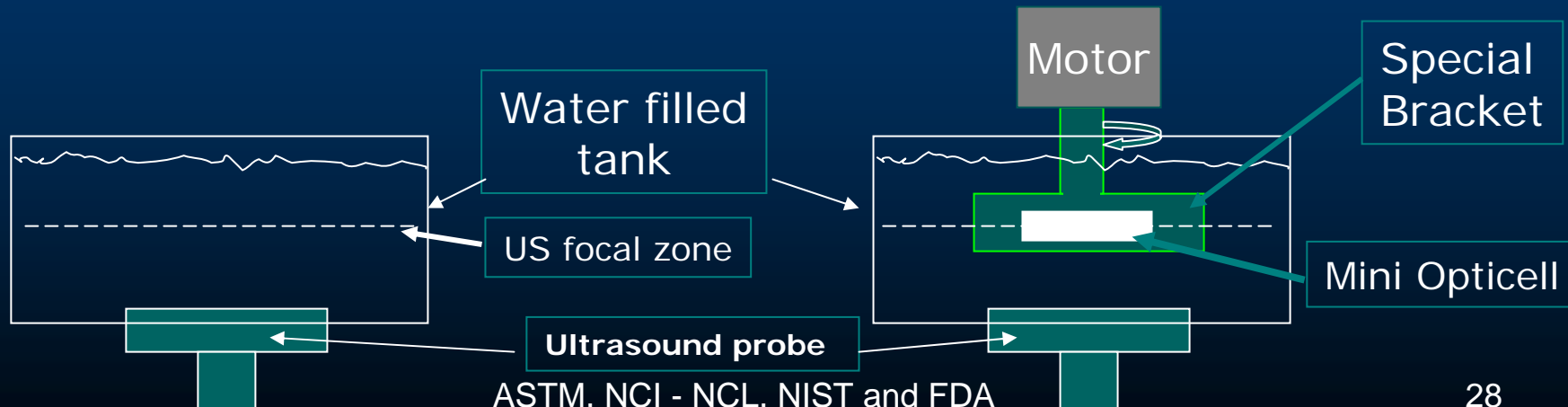
# In Vitro Tests



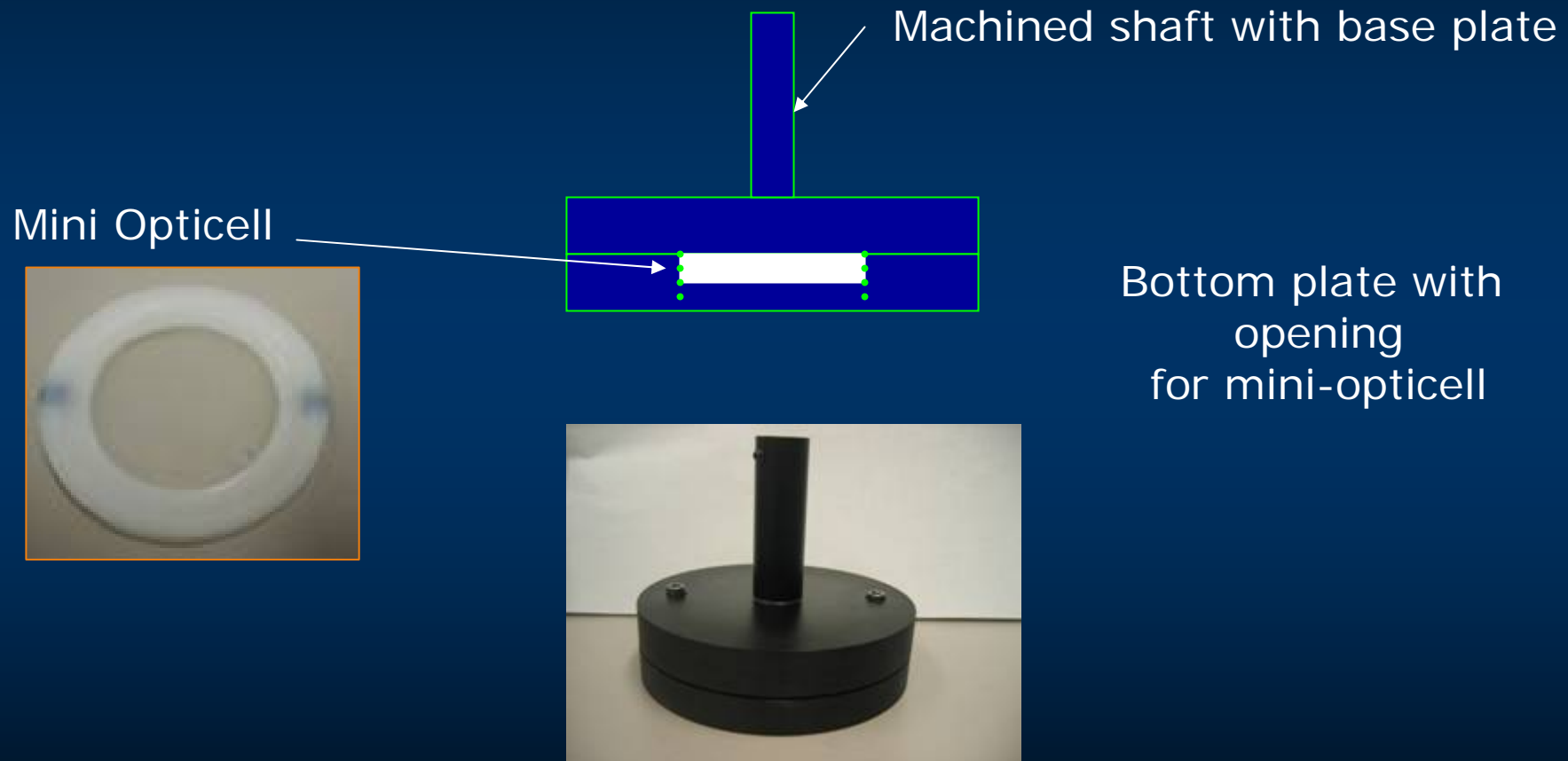
# In Vitro Tests of Insonation Strategy using Ultrasound

- Requirements
  1. Precise positioning of Mini Opticell in the prescribed regions of the ultrasound probe focal zone(s)
  2. Complete insonation of all the cells within the Mini Opticell

SOLUTION = SLOWLY ROTATE THE MINI OPTICELL IN THE ULTRASOUND FOCAL ZONE

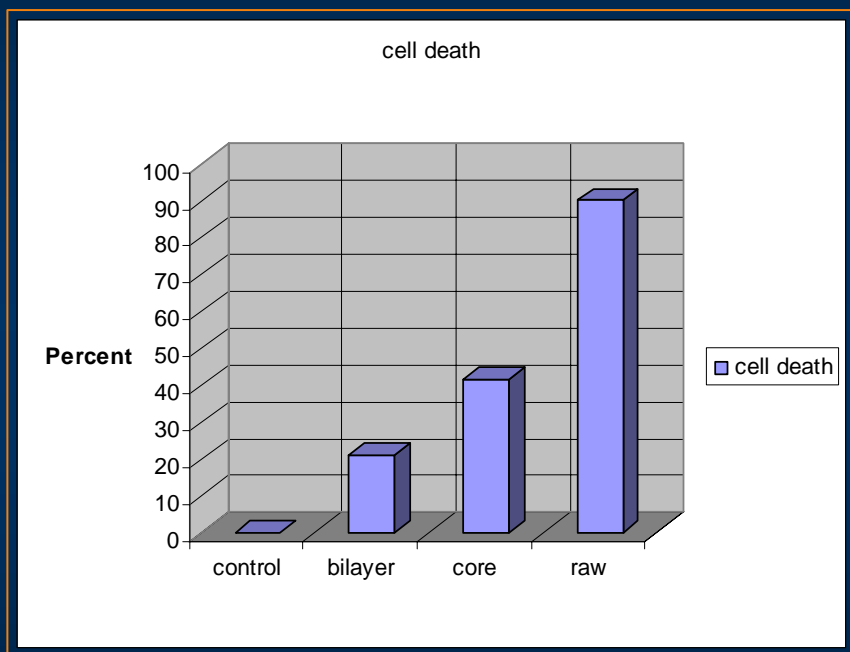


# Mini Opticell Bracket Basic Design

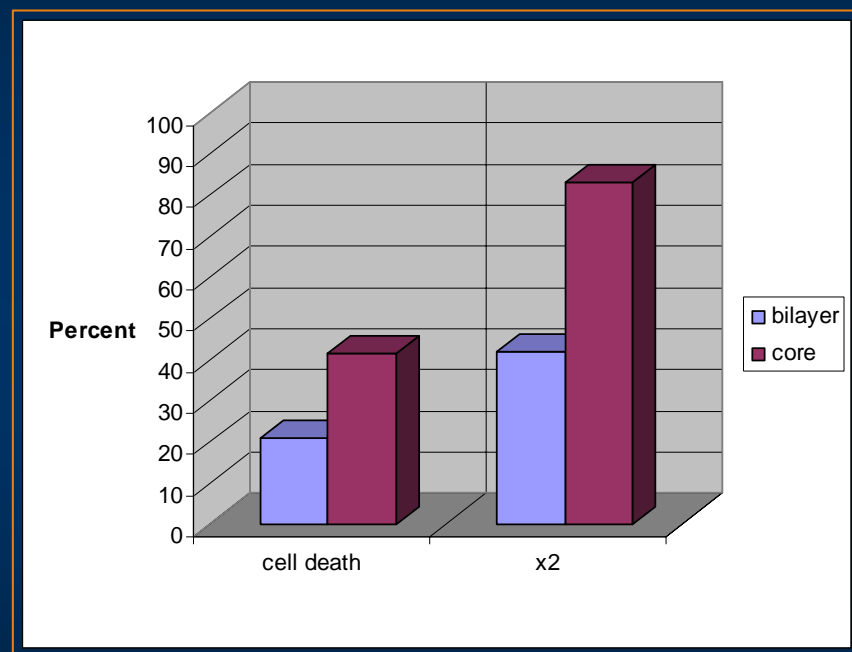


# In Vitro Tests HT 29

A Single Dose Test

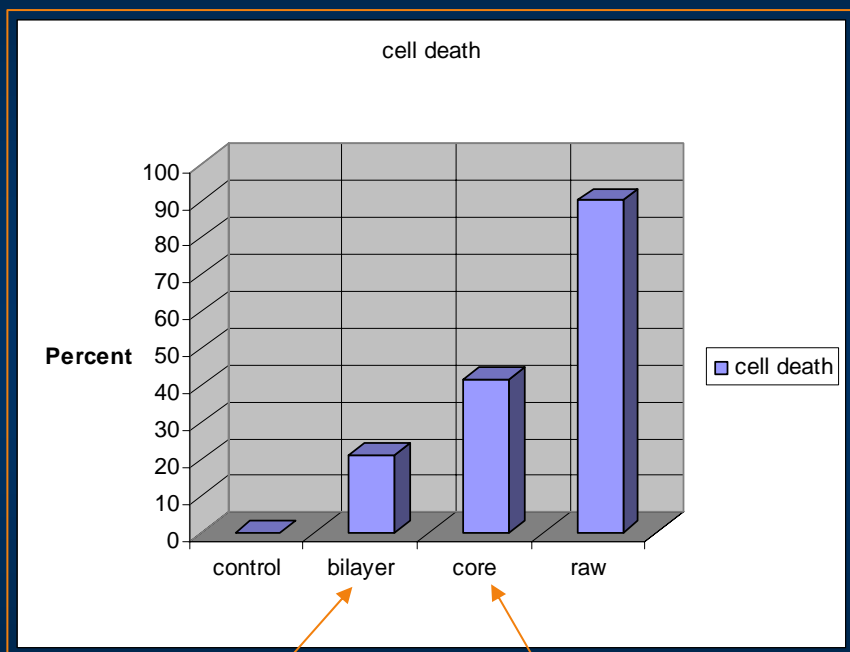


B



# In Vitro Tests

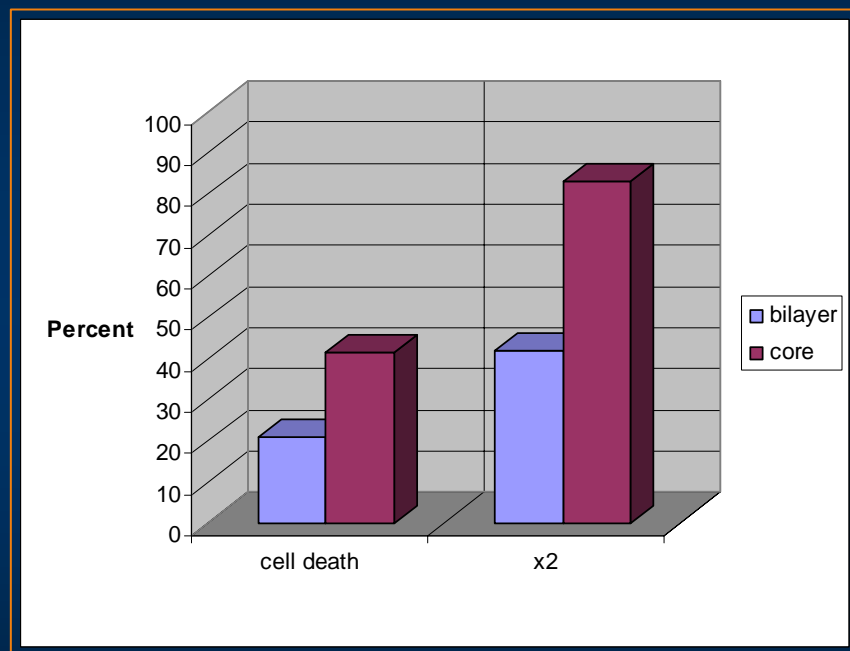
A Single Dose Test



Taxotere

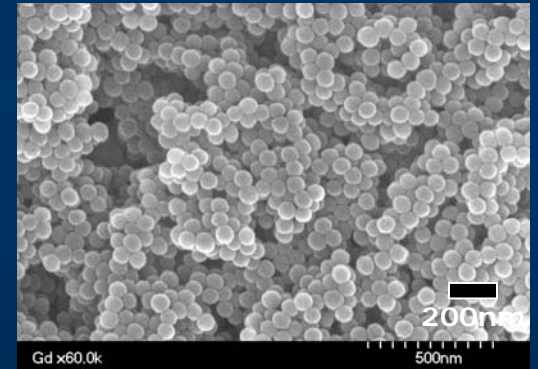
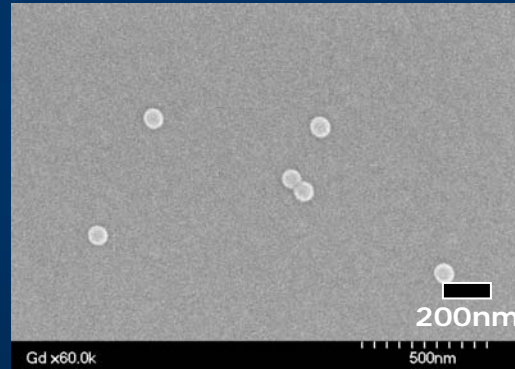
Adriamycin

B

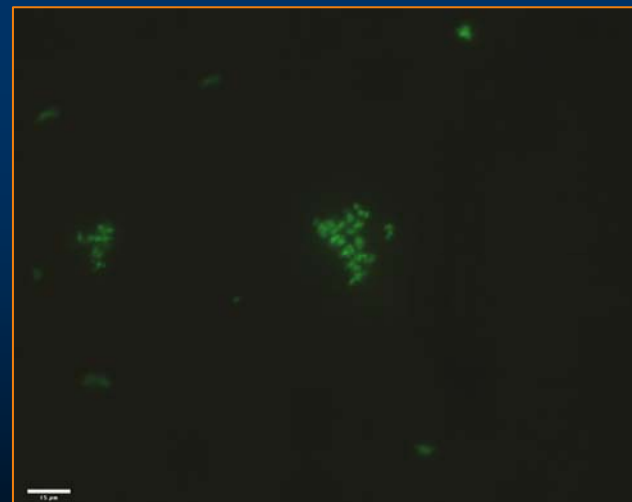
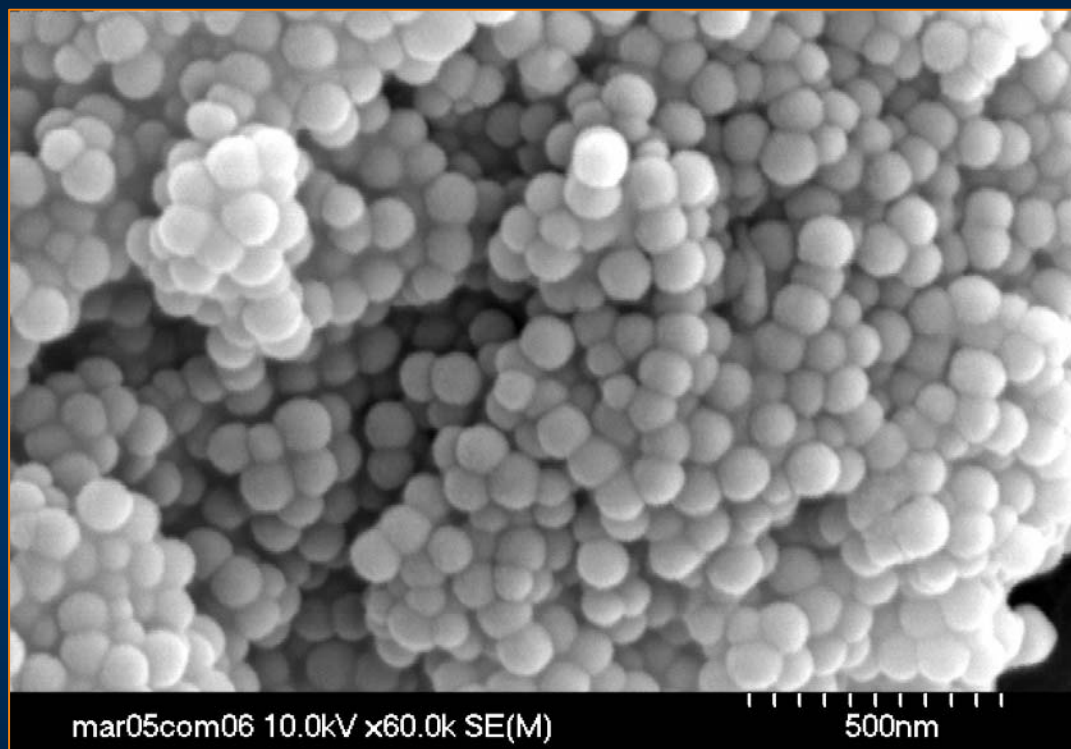


# Silica Nanoparticle (SiO-NP)

- Choi, Watkin, Kim
- $\text{SiO}_2$
- 20 nm – 200nm
- Doped  
Gd DTPA  
CF



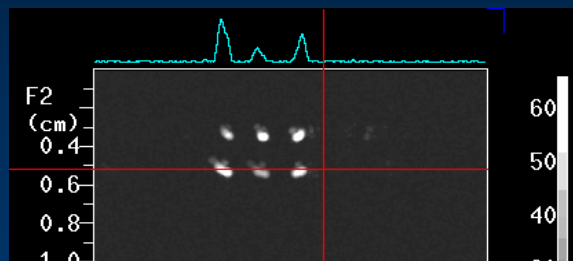
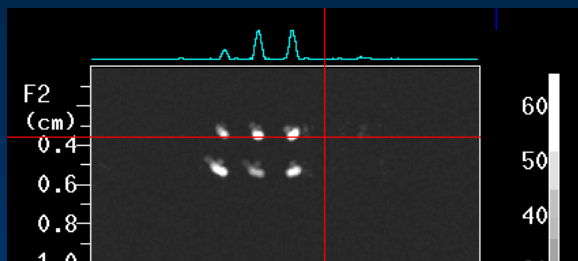
# Silica Nanoparticles (SiO-NP)



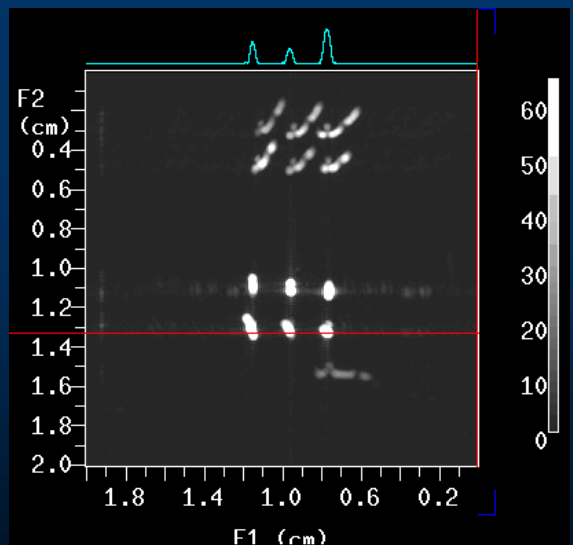
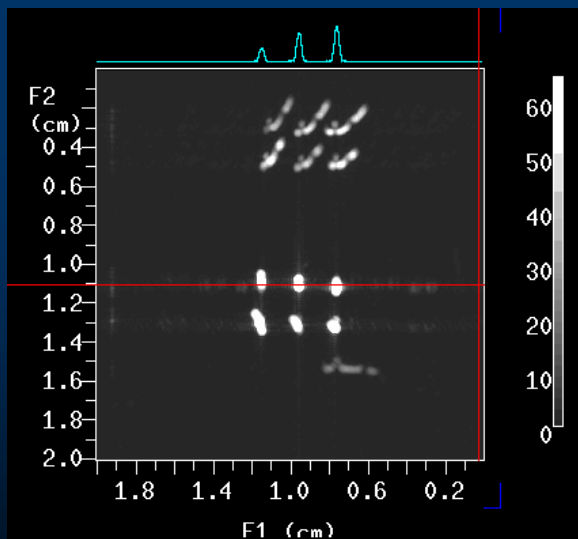
# 14 T MR images (SiO-NP)

Contrast intensity

Tr=0.1sec



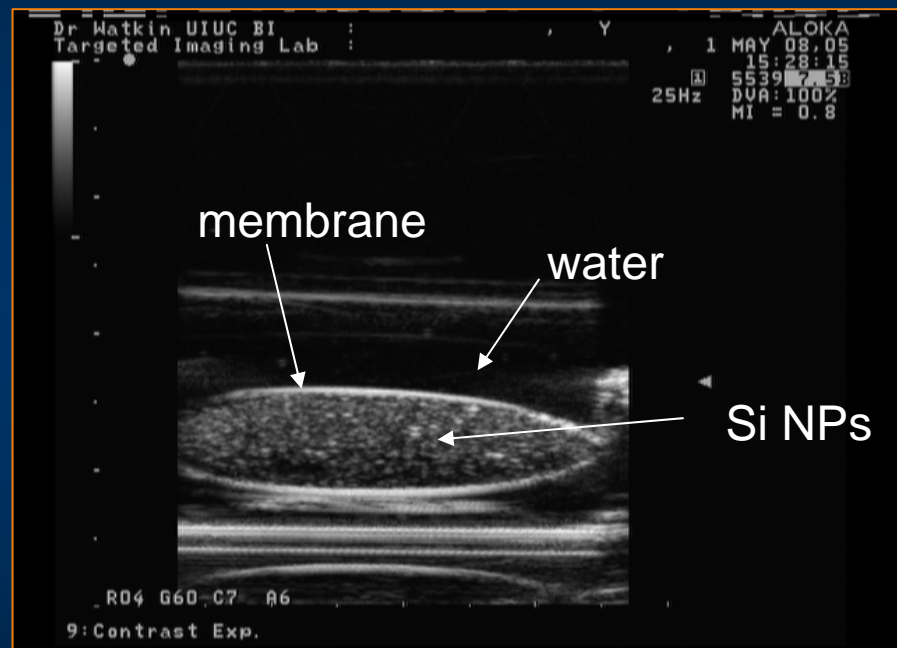
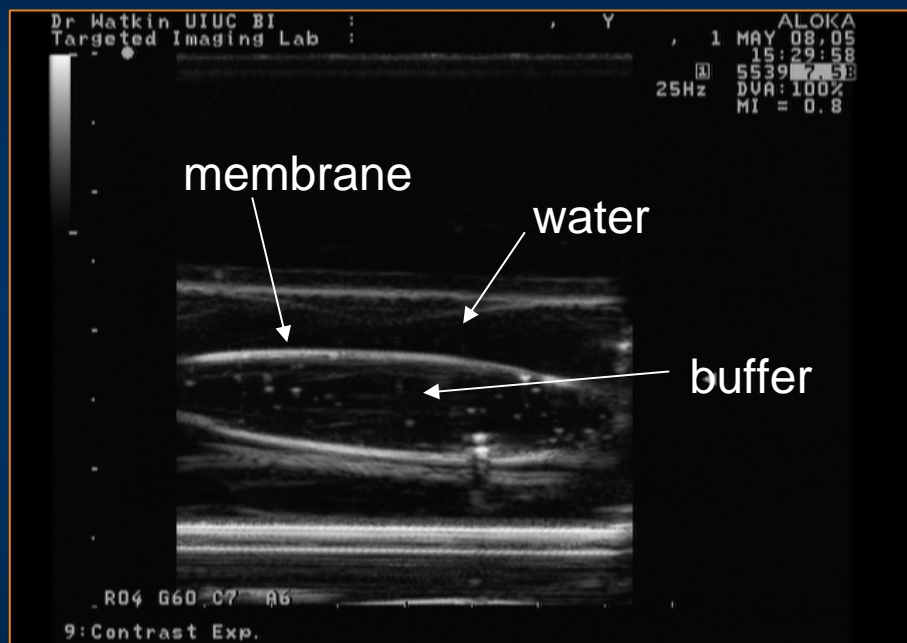
Tr=0.5sec



**Low** concentration samples

**High** concentration samples

# Ultrasound (SiO-NP)



# Silica Nanoparticles

- Characteristics
  - ? Toxicity
  - ? Biodistribution
  - ? Pharmacokinetics
- Current Study Pathway
  - Biodistribution
  - LD<sub>50</sub>

# Summary

- Controlled release nanoparticles
  - Watkin & Gosangari, Controlled Release Society, Miami, FL, June 2005
- Functionalized CR-NPs
  - Individualizeable
- Small Ultrasonic Imaging System for use with CR-NPs
  - *“point and shoot”*
- Loadable -- drugs ...
  - Multiple i.e. Taxotere & Doxorubicin

